

AMENDMENTS TO THE CLAIMS

1-46. (canceled)

47. (withdrawn): A method for producing antibodies to a three-dimensional epitope of a bioactive human parathyroid hormone, comprising:

- a) immunizing an animal with the bioactive human parathyroid hormone; and
- b) recovering antibodies from the animal; whereby the antibodies specifically recognize the three-dimensional structure of the bioactive human parathyroid hormone.

48. (withdrawn): The method of claim 47, further comprising immunizing the animal with the human parathyroid hormone a second time before recovering the antibodies from the animal.

49. (withdrawn): The method of claim 47, wherein the human parathyroid hormone is coupled to a carrier.

50. (withdrawn): The method of claim 49, wherein the carrier is keyhole limpet hemocyanin.

51. (withdrawn): The method of claim 47, wherein the bioactive human parathyroid hormone comprises SEQ ID NO: 1.

52. (withdrawn): The method of claim 47, further comprising isolating the antibodies.

53. (withdrawn): The method of claim 52, wherein the antibodies are isolated by affinity chromatography.

54. (withdrawn): The method of claim 53, wherein the antibodies are isolated by screening the antibodies with fragments of the human parathyroid hormone linked to a solid phase.

55. (withdrawn): A method for producing antibodies that recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone, comprising

- a) immunizing an animal with parathyroid hormone;
- b) immunizing the animal with parathyroid hormone a second time; and
- c) recovering the antibodies from the animal,

whereby the antibodies recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone.

56. (withdrawn): The method of claim 55, wherein the parathyroid hormone is conjugated to a carrier.

57. (withdrawn): The method of claim 56, wherein the carrier is keyhole limpet hemocyanin.

58. (withdrawn): The method of claim 54, wherein the parathyroid hormone is human parathyroid hormone.

59. (withdrawn): The method of claim 55, further comprising isolating the antibodies so recovered.

60. (withdrawn): The method of claim 59, wherein the antibodies are isolated by affinity chromatography.

61. (withdrawn): The method of claim 60, wherein the antibodies are isolated by fragments of parathyroid hormone coupled to a solid phase.

62. (withdrawn): The method of claim 61, wherein the fragments of parathyroid hormone are selected from the group consisting of amino acids 1-13, 13-34, and 39-84 of SEQ ID NO: 1.

63. (withdrawn): The method of claim 61, wherein the antibodies are isolated by a fragment of parathyroid hormone consisting of amino acids 1-13 of SEQ ID NO: 1.

64. (withdrawn): A method for producing antibodies that recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone, comprising

a) immunizing an animal with parathyroid hormone, wherein the parathyroid hormone comprises amino acids 1-84 of SEQ ID NO: 1;

b) immunizing the animal with parathyroid hormone a second time; and

c) recovering the antibodies from the animal,

whereby the antibodies recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone.

65. (withdrawn): The method of claim 64, further comprising isolating the antibodies so recovered.

66. (withdrawn): The method of claim 64, wherein the bioactive three-dimensional epitope of parathyroid hormone consists of amino acids 1-13 of SEQ ID NO: 1.

67. (withdrawn): A method for producing antibodies that recognize and bind the bioactive, three-dimensional amino terminus of parathyroid hormone, comprising

a) immunizing an animal with parathyroid hormone conjugated to a keyhole limpet hemocyanin, wherein the parathyroid hormone comprises amino acids 1-84 of SEQ ID NO: 1;

b) subsequently immunizing the animal with parathyroid hormone; and

c) recovering the antibodies from the animal,

whereby the antibodies recognize and bind the bioactive, three-dimensional amino terminus of parathyroid hormone.

68. (withdrawn): The method of claim 67, wherein the bioactive three-dimensional amino terminus of parathyroid hormone consists of amino acids 1-13 of SEQ ID NO: 1.

69. (currently amended): An isolated antibody that specifically binds to a bioactive, ~~three-dimensional~~ epitope of a parathyroid hormone (PTH) in PTH₁₋₈ or PTH₁₋₉ sequence, wherein said isolated antibody binds to said ~~three-dimensional~~ epitope within a whole PTH with a higher affinity than its binding to said ~~three-dimensional~~ epitope within a PTH fragment selected from the group consisting of a PTH₁₋₈ fragment, a PTH₁₋₉ fragment, a PTH₁₋₁₀ fragment, and to a PTH₁₋₃₄ fragment, and said isolated antibody does not specifically bind to a non-(1-84) PTH fragment.

70. (currently amended): The isolated antibody of claim 69, wherein the bioactive, ~~three-dimensional~~ epitope is in PTH₁₋₈ sequence.

71. (previously presented): The isolated antibody of claim 69, wherein the parathyroid hormone is human parathyroid hormone.

72-77. (canceled)

78. (currently amended): A therapeutic composition comprising an isolated antibody that specifically binds to a bioactive, ~~three-dimensional~~ epitope of a parathyroid hormone (PTH) in PTH₁₋₈ or PTH₁₋₉ sequence, wherein said isolated antibody binds to said ~~three-dimensional~~ epitope within a whole PTH with a higher affinity than its binding to said ~~three-dimensional~~ epitope within a PTH fragment selected from the group consisting of a PTH₁₋₈ fragment, a PTH₁₋₉ fragment, a PTH₁₋₁₀ fragment, and to a PTH₁₋₃₄ fragment, and said isolated antibody does not specifically bind to a non-(1-84) PTH fragment, and a pharmaceutically-acceptable carrier.

79. (currently amended): The antibody of claim 69, wherein the antibody reduces adenylate cyclase activity by binding to the ~~three-dimensional~~ bioactive epitope of the parathyroid hormone.

80. (previously presented): The antibody of claim 69, wherein the antibody is a polyclonal antibody.

81. (previously presented): The antibody of claim 69, wherein the antibody is a monoclonal antibody.

82. (previously presented): The antibody of claim 69, wherein the antibody is a humanized antibody.

83. (previously presented): The antibody of claim 69, wherein the antibody is an antibody fragment.

84. (previously presented): The antibody of claim 69, which is coupled to a detectable marker.

85. (canceled)

86. (currently amended): An isolated polyclonal antibody that specifically binds to a bioactive ~~three-dimensional~~ epitope of human parathyroid hormone (PTH) produced by a process comprising the following steps:

- a) immunizing an animal with human whole PTH as a primary immunization;
- b) immunizing said animal with human whole PTH subsequent to said primary immunization;
- c) recovering a polyclonal antibody from said animal, and
- d) isolating said polyclonal antibody by binding said polyclonal antibody to at least four amino acids in the common sequence of human and rat PTH (1-8) sequence,

whereby said polyclonal antibody specifically binds to said bioactive ~~three-dimensional~~ epitope of human PTH with a higher affinity than its binding to said ~~three-dimensional~~ bioactive epitope within a PTH fragment selected from the group consisting of a PTH₁₋₈ fragment, a PTH₁₋₉ fragment, a PTH₁₋₁₀ fragment, and ~~to~~ a PTH₁₋₃₄ fragment.

87-91. (canceled)

92. (currently amended): A kit comprising an isolated antibody that specifically binds to a bioactive, ~~three-dimensional~~ epitope of parathyroid hormone (PTH) in PTH₁₋₈ or PTH₁₋₉ sequence, wherein said isolated antibody binds to said ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to said ~~three-dimensional~~ bioactive epitope within a PTH fragment selected from the group consisting of a PTH₁₋₈ fragment, a PTH₁₋₉ fragment, a PTH₁₋₁₀ fragment, and ~~to~~ a PTH₁₋₃₄ fragment and said isolated antibody does not specifically bind to a non-(1-84) PTH fragment.

93. (previously presented): The kit of claim 92, wherein the antibody is coupled with a detectable label.

94. (canceled)

95. (previously presented): The kit of claim 92, further comprising a tool for obtaining a biological sample containing parathyroid hormone from a patient.

96. (previously presented): The kit of claim 93, wherein the detectable label is selected from the group consisting of a chemiluminescent marker, a fluorescent marker, a radioactive marker, and an enzymatic marker.

97. (previously presented): The kit of claim 93, wherein the detectable label is an acridinium ester.

98. (withdrawn): A method for detecting bioactive parathyroid hormone in a sample, comprising

- a) exposing the sample to an antibody that recognizes and binds the bioactive three-dimensional epitope of parathyroid hormone; and
- b) detecting the antibody-hormone complex, thereby detecting the bioactive parathyroid hormone in the sample.

99. (withdrawn): The method of claim 98, wherein the antibody that recognizes and binds the bioactive three-dimensional epitope of parathyroid hormone is coupled with a detectable marker.

100. (withdrawn): The method of claim 98, further comprising exposing the antibody-hormone complex to another antibody that recognizes and binds parathyroid hormone before step (b).

101. (withdrawn): A method for detecting bioactive parathyroid hormone in a sample, comprising

- a) exposing the sample to a capture antibody that recognizes and binds the bioactive three-dimensional epitope of parathyroid hormone;
- b) exposing the capture antibody-hormone complex to a detection antibody that binds a different epitope than the capture antibody; and
- b) detecting the antibody-hormone complex, thereby detecting the bioactive parathyroid hormone in the sample.

102. (withdrawn): The method of claim 101, wherein the detection antibody is coupled to a chemiluminescent marker.

103. (withdrawn): The method of claim 102, wherein the chemiluminescent marker is an acridinium ester.

104. (withdrawn): The method of claim 98, wherein the sample is from a patient with hyperparathyroidism or hypoparathyroidism.

105. (withdrawn): The method of claim 101, wherein the sample is from a patient with hyperparathyroidism or hypoparathyroidism.

106. (withdrawn): An immunoassay comprising an antibody that recognizes and binds the bioactive three-dimensional amino terminus of human parathyroid hormone.

107. (withdrawn): The immunoassay of claim 106, wherein the bioactive three-dimensional amino terminus consists of amino acids 1-13 of SEQ ID NO: 1.

108. (currently amended): The isolated antibody of claim 69, wherein the bioactive, ~~three dimensional~~ epitope is in PTH₁₋₉ sequence.

109. (currently amended): The isolated antibody of claim 69, which isolated antibody binds to the ~~three dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three dimensional~~ bioactive epitope within a PTH₁₋₈ fragment.

110. (currently amended): The isolated antibody of claim 69, which the isolated antibody binds to the ~~three dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three dimensional~~ bioactive within a PTH₁₋₉ fragment.

111. (currently amended): The isolated antibody of claim 69, which isolated antibody binds to the ~~three dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three dimensional~~ bioactive epitope within a PTH₁₋₃₄ fragment.

112. (currently amended): The isolated antibody of claim 69, wherein the bioactive, ~~three dimensional~~ epitope is in PTH₁₋₉ sequence and the isolated antibody binds to the ~~three dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three dimensional~~ bioactive epitope within the PTH₁₋₉ fragment.

113. (previously presented): The isolated antibody of claim 69, wherein the non-(1-84) PTH fragment is a PTH₇₋₈₄ fragment.

114. (currently amended): The therapeutic composition of claim 78, wherein the bioactive, ~~three-dimensional~~ epitope is in PTH₁₋₈ sequence.

115. (currently amended): The therapeutic composition of claim 78, wherein the bioactive, ~~three-dimensional~~ epitope is in PTH₁₋₉ sequence.

116. (currently amended): The therapeutic composition of claim 78, wherein the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within a PTH₁₋₈ fragment.

117. (currently amended): The therapeutic composition of claim 78, wherein the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within a PTH₁₋₉ fragment.

118. (currently amended): The therapeutic composition of claim 78, wherein the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within a PTH₁₋₃₄ fragment.

119. (currently amended): The therapeutic composition of claim 78, wherein the bioactive, ~~three-dimensional~~ epitope is in PTH₁₋₉ sequence and the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within the PTH₁₋₉ fragment.

120. (previously presented): The therapeutic composition of claim 78, wherein the non-(1-84) PTH fragment is a PTH₇₋₈₄ fragment.

121. (currently amended): The kit of claim 92, wherein the bioactive, ~~three-dimensional~~ epitope is in PTH₁₋₈ sequence.

122. (currently amended): The kit of claim 92, wherein the bioactive, ~~three-dimensional~~ epitope is in PTH₁₋₉ sequence.

123. (currently amended): The kit of claim 92, wherein the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within a PTH₁₋₈ fragment.

124. (currently amended): The kit of claim 92, wherein the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within a PTH₁₋₉ fragment.

125. (currently amended): The kit of claim 92, wherein the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within a PTH₁₋₃₄ fragment.

126. (currently amended): The kit of claim 92, wherein the bioactive, ~~three-dimensional~~ epitope is in PTH₁₋₉ sequence and the isolated antibody binds to the ~~three-dimensional~~ bioactive epitope within a whole PTH with a higher affinity than its binding to the ~~three-dimensional~~ bioactive epitope within the PTH₁₋₉ fragment.

127. (previously presented): The kit of claim 92, wherein the non-(1-84) PTH fragment is a PTH₇₋₈₄ fragment.

128. (new): The isolated antibody of claim 69, which isolated antibody binds to the bioactive epitope within a whole PTH with a higher affinity than its binding to the bioactive epitope within a PTH₁₋₁₀ fragment.

129. (new): The therapeutic composition of claim 78, wherein the isolated antibody binds to the bioactive epitope within a whole PTH with a higher affinity than its binding to the bioactive epitope within a PTH₁₋₁₀ fragment.

130. (new): The isolated polyclonal antibody of claim 86, which isolated polyclonal antibody binds to the bioactive epitope within a whole PTH with a higher affinity than its binding to the bioactive epitope within a PTH₁₋₁₀ fragment.

131. (new): The kit of claim 92, wherein the isolated antibody binds to the bioactive epitope within a whole PTH with a higher affinity than its binding to the bioactive epitope within a PTH₁₋₁₀ fragment.